10992_29 ST25.txt
SEQUENCE LISTING

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       Davignon, Jean

<120> MAMMALIAN SUBTILISIN/KEXIN ISOZYME SKI-1: A PROPROTEIN CONVERTASE
       WITH A UNIQUE CLEAVAGE SPECIFICITY

<130> 10992.29

<140> US 09/830,837
<141> 1999-11-04

<150> PCT/CA1999/01058
<151> 1999-11-04

<150> CA 2,249,648
<151> 1998-11-04

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Page 1

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Gln Glu Thr Ala Val Val Asp Asn Val Pro Ile Leu Gly Leu Tyr Gln
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gga gcc  atg gtg gcc ctg gcc  ttc ttc gtg gta cag  atc agt aag       3486
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Glu Val Asp Asn Trp Arg Ile Ile Pro Arg Asn Asn Pro Ser Ser Asp
                85   90   95

Tyr Pro Ser Asp Phe Glu Val Ile Gln Ile Lys Glu Lys Gln Lys Ala
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Gly Leu Leu Thr Leu Glu Asp His Pro Asn Ile Lys Arg Val Thr Pro
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Gln Arg Lys Val Phe Arg Ser Leu Lys Phe Ala Glu Ser Asp Pro Ile
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Val Pro Cys Asn Glu Thr Arg Trp Ser Gln Lys Trp Gln Ser Ser Arg
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Gly Ala Asn Val Arg Val Ala Val Phe Asp Thr Gly Leu Ser Glu Lys
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His Pro His Phe Lys Asn Val Lys Glu Arg Thr Asn Trp Thr Asn Glu
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Arg Thr Leu Asp Asp Gly Leu Gly His Gly Thr Phe Val Ala Gly Val
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Ile Ala Ser Met Arg Glu Cys Gln Gly Phe Ala Pro Asp Ala Glu Leu
            260             265             270

His Ile Phe Arg Val Phe Thr Asn Asn Gln Val Ser Tyr Thr Ser Trp
        275             280             285

Phe Leu Asp Ala Phe Asn Tyr Ala Ile Leu Lys Lys Met Asp Val Leu
    290             295             300

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Gly Asn Asp Gly Pro Leu Tyr Gly Thr Leu Asn Asn Pro Ala Asp Gln
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Ser Gly Val Lys Gly Gly Cys Arg Ala Leu Ser Gly Thr Ser Val Ala
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Ser Ala Arg Arg Leu Pro Gly Val Asn Met Phe Glu Gln Gly His Gly
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Val Val Phe Ser Asp Trp Tyr Asn Thr Ser Val Met Arg Lys Val Lys
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Met Tyr Tyr Ala Ser Gly Cys Ser Ile Ala Arg Phe Pro Glu Asp Gly
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Val Val Ile Thr Gln Thr Phe Lys Asp Gln Gly Leu Glu Val Leu Lys
         805           810           815

Gln Glu Thr Ala Val Val Asp Asn Val Pro Ile Leu Gly Leu Tyr Gln
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Ile Pro Ala Glu Gly Gly Gly Arg Ile Val Leu Tyr Gly Asp Ser Asn
      835             840          845

Cys Leu Asp Asp Ser His Arg Gln Lys Asp Cys Phe Trp Leu Leu Asp
  850               855          860

Ala Leu Leu Gln Tyr Thr Ser Tyr Gly Val Thr Pro Pro Ser Leu Ser
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His Ser Gly Asn Arg Gln Arg Pro Pro Ser Gly Ala Gly Leu Ala Pro
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Leu Cys Gly Lys Arg His Leu Gly Asp Arg Leu Gly Thr Arg Ala Leu
15              20              25              30


gaa aag gcc ccg tgc ccc agc tgc tcc cac ctg act ttg aag gtg gaa      145
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Tyr Phe Thr Ala Lys Ala Arg Asn Ser Phe Ile Ser Ser Ala Leu Lys
            65              70              75

agc agt gaa gtg gaa aac tgg aga ata ata cct cgg aac aac cca tcc    289
Ser Ser Glu Val Glu Asn Trp Arg Ile Ile Pro Arg Asn Asn Pro Ser
            80              85              90

agt gac tac cct agt gat ttt gag gtg att cag ata aaa gag aag cag    337
Ser Asp Tyr Pro Ser Asp Phe Glu Val Ile Gln Ile Lys Glu Lys Gln
95              100             105             110

aag gcg ggg ctg ctc aca ctt gaa gat cac ccc aac atc aag cgg gtg    385
Lys Ala Gly Leu Leu Thr Leu Glu Asp His Pro Asn Ile Lys Arg Val
                115             120             125

aca ccc cag cgg aaa gtc ttt cgt tcc ctc aag ttt gct gaa tcc aac    433
Thr Pro Gln Arg Lys Val Phe Arg Ser Leu Lys Phe Ala Glu Ser Asn
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ccc atc gtg ccc tgt aat gaa acc cgg tgg agc cag aag tgg cag tca    481
Pro Ile Val Pro Cys Asn Glu Thr Arg Trp Ser Gln Lys Trp Gln Ser
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tca cgt ccc ctg aaa aga gcc agt ctc tcc ctg ggc tct gga ttc tgg    529
Ser Arg Pro Leu Lys Arg Ala Ser Leu Ser Leu Gly Ser Gly Phe Trp
160             165             170

cat gca aca gga aga cat tca agt cgg cga ttg ctg aga gcc att cct    577
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175             180             185             190

cgc cag gtc gcc cag aca ctg cag gca gat gtg ctg tgg cag atg gga    625
Arg Gln Val Ala Gln Thr Leu Gln Ala Asp Val Leu Trp Gln Met Gly
                195             200             205

tac aca ggt gct aat gtc aga gtt gct gtt ttt gat act ggg ctc agt    673
Tyr Thr Gly Ala Asn Val Arg Val Ala Val Phe Asp Thr Gly Leu Ser
                210             215             220

gag aag cat ccg cat ttt aag aat gtg aag gag aga acc aac tgg acc    721
Glu Lys His Pro His Phe Lys Asn Val Lys Glu Arg Thr Asn Trp Thr
            225             230             235

aat gag cgg acc ctg gat gat ggg cta ggc cat ggc aca ttc gtt gca    769
Asn Glu Arg Thr Leu Asp Asp Gly Leu Gly His Gly Thr Phe Val Ala
240             245             250

ggt gtg att gcc agc atg agg gag tgc caa gga ttt gct cca gat gca    817
Gly Val Ile Ala Ser Met Arg Glu Cys Gln Gly Phe Ala Pro Asp Ala
255             260             265             270

gag ctg cac atc ttc agg gtc ttt acc aac aat cag gtg tct tac aca    865
Glu Leu His Ile Phe Arg Val Phe Thr Asn Asn Gln Val Ser Tyr Thr
                275             280             285

tct tgg ttt ctg gat gcc ttc aac tat gcc atc cta aag aag atg gac    913
Ser Trp Phe Leu Asp Ala Phe Asn Tyr Ala Ile Leu Lys Lys Met Asp
            290             295             300
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gtt ctc aac ctt agc atc ggt ggg ccc gac ttc atg gat cat ccg ttt      961
Val Leu Asn Leu Ser Ile Gly Gly Pro Asp Phe Met Asp His Pro Phe
        305                 310                 315

gtt gac aag gtg tgg gaa tta aca gct aac aat gta att atg gtt tct     1009
Val Asp Lys Val Trp Glu Leu Thr Ala Asn Asn Val Ile Met Val Ser
        320                 325                 330

gct att ggc aat gat gga cct ctc tat ggc act ctg aat aac cct gct     1057
Ala Ile Gly Asn Asp Gly Pro Leu Tyr Gly Thr Leu Asn Asn Pro Ala
335                 340                 345                 350

gat cag atg gat gtg att gga gtg ggt ggc att gac ttt gaa gat aac     1105
Asp Gln Met Asp Val Ile Gly Val Gly Gly Ile Asp Phe Glu Asp Asn
                355                 360                 365

atc gct cgc ttt tct tcc agg gga atg act acc tgg gaa tta cca gga     1153
Ile Ala Arg Phe Ser Ser Arg Gly Met Thr Thr Trp Glu Leu Pro Gly
                370                 375                 380

ggc tat ggt cgt gtg aag cct gac att gtc acc tat ggt gct gga gtg     1201
Gly Tyr Gly Arg Val Lys Pro Asp Ile Val Thr Tyr Gly Ala Gly Val
        385                 390                 395

cgg ggt tcc ggt gtg aaa ggg ggc tgc cgt gca ctc tca ggg acc agt     1249
Arg Gly Ser Gly Val Lys Gly Gly Cys Arg Ala Leu Ser Gly Thr Ser
        400                 405                 410

gtc gct tcc cca gtg gtc gct ggg gcc gtc acc ttg tta gta agc aca     1297
Val Ala Ser Pro Val Val Ala Gly Ala Val Thr Leu Leu Val Ser Thr
415                 420                 425                 430

gta cag aag cgg gag ctg gtg aat cct gcc agt gtg aag caa gct ttg     1345
Val Gln Lys Arg Glu Leu Val Asn Pro Ala Ser Val Lys Gln Ala Leu
                435                 440                 445

ata gcg tca gcc cgg aga ctt cct ggg gtc aac atg ttc gag caa ggt     1393
Ile Ala Ser Ala Arg Arg Leu Pro Gly Val Asn Met Phe Glu Gln Gly
                450                 455                 460

cat ggc aag ttg gat ctg ctg cga gct tat cag atc ctc agc agc tat     1441
His Gly Lys Leu Asp Leu Leu Arg Ala Tyr Gln Ile Leu Ser Ser Tyr
                465                 470                 475

aaa ccg cag gca agc ctg agt cct agc tac atc gac ctg act gag tgt     1489
Lys Pro Gln Ala Ser Leu Ser Pro Ser Tyr Ile Asp Leu Thr Glu Cys
        480                 485                 490

ccc tac atg tgg ccc tac tgc tcc cag cct atc tac tat gga gga atg     1537
Pro Tyr Met Trp Pro Tyr Cys Ser Gln Pro Ile Tyr Tyr Gly Gly Met
495                 500                 505                 510

cca aca atc gtt aat gtc acc atc ctc aat ggc atg ggc gtc aca gga     1585
Pro Thr Ile Val Asn Val Thr Ile Leu Asn Gly Met Gly Val Thr Gly
                515                 520                 525

aga att gtg gat aag cct gag tgg cga ccc tat tta cca cag aat gga     1633
Arg Ile Val Asp Lys Pro Glu Trp Arg Pro Tyr Leu Pro Gln Asn Gly
                530                 535                 540

gac aac att gaa gtg gcc ttc tcc tac tcc tca gtg ttg tgg ccc tgg     1681
Asp Asn Ile Glu Val Ala Phe Ser Tyr Ser Ser Val Leu Trp Pro Trp
                545                 550                 555
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tca ggt tac ctt gcc atc tcc att tct gtg acc aag aag gca gct tcc     1729
Ser Gly Tyr Leu Ala Ile Ser Ile Ser Val Thr Lys Lys Ala Ala Ser
        560             565             570

tgg gaa ggc atc gct cag ggc cac atc atg atc aca gtg gcg tcc cca     1777
Trp Glu Gly Ile Ala Gln Gly His Ile Met Ile Thr Val Ala Ser Pro
575             580             585             590


gca gag aca gag tta cac agt ggt gcg gag cac act tcc acc gtg aag     1825
Ala Glu Thr Glu Leu His Ser Gly Ala Glu His Thr Ser Thr Val Lys
                595             600             605

ctg ccc atc aag gtg aag atc att ccc acc cct cct cgg agc aag aga     1873
Leu Pro Ile Lys Val Lys Ile Ile Pro Thr Pro Pro Arg Ser Lys Arg
                610             615             620

gtc ctc tgg gac cag tac cac aac ctc cgc tac cca cct ggc tac ttc     1921
Val Leu Trp Asp Gln Tyr His Asn Leu Arg Tyr Pro Pro Gly Tyr Phe
        625             630             635

ccc agg gac aac ttg cgg atg aag aat gac cct tta gac tgg aat ggc     1969
Pro Arg Asp Asn Leu Arg Met Lys Asn Asp Pro Leu Asp Trp Asn Gly
        640             645             650

gac cac gtc cac acc aac ttc agg gac atg tac cag cat ctg cgc agc     2017
Asp His Val His Thr Asn Phe Arg Asp Met Tyr Gln His Leu Arg Ser
655             660             665             670

atg ggc tac ttc gtg gag gtg ctc ggc gcc cca ttc aca tgt ttt gac     2065
Met Gly Tyr Phe Val Glu Val Leu Gly Ala Pro Phe Thr Cys Phe Asp
                675             680             685

gcc aca cag tat ggc act ttg ctg ctg gtg gac agt gag gaa gag tac     2113
Ala Thr Gln Tyr Gly Thr Leu Leu Leu Val Asp Ser Glu Glu Glu Tyr
                690             695             700

ttc cct gag gag att gct aag ctg agg agg gat gtg gac aat ggc ctt     2161
Phe Pro Glu Glu Ile Ala Lys Leu Arg Arg Asp Val Asp Asn Gly Leu
                705             710             715

tcc ctc gtc atc ttc agt gac tgg tac aac act tct gtt atg aga aaa     2209
Ser Leu Val Ile Phe Ser Asp Trp Tyr Asn Thr Ser Val Met Arg Lys
        720             725             730

gtg aag ttt tat gat gaa aac acc agg cag tgg tgg atg cca gac acc     2257
Val Lys Phe Tyr Asp Glu Asn Thr Arg Gln Trp Trp Met Pro Asp Thr
735             740             745             750

gga gga gcg aac atc cca gct ctg aat gag ctg ctg tct gtg tgg aac     2305
Gly Gly Ala Asn Ile Pro Ala Leu Asn Glu Leu Leu Ser Val Trp Asn
                755             760             765

atg ggg ttc agt gac ggc cta tat gaa ggg gag ttt gtc ctg gca aac     2353
Met Gly Phe Ser Asp Gly Leu Tyr Glu Gly Glu Phe Val Leu Ala Asn
                770             775             780

cat gac atg tac tat gcg tcg ggg tgc agc atc gcc aag ttt cca gaa     2401
His Asp Met Tyr Tyr Ala Ser Gly Cys Ser Ile Ala Lys Phe Pro Glu
                785             790             795
```

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gat ggc gtc gtg atc aca cag act ttc aag gac caa gga ttg gag gtc    2449
Asp Gly Val Val Ile Thr Gln Thr Phe Lys Asp Gln Gly Leu Glu Val
    800             805             810

tta aaa caa gag aca gca gtt gtg gaa aat gtt ccc att ttg ggg ctt    2497
Leu Lys Gln Glu Thr Ala Val Val Glu Asn Val Pro Ile Leu Gly Leu
815             820             825             830

tat cag att cca tct gaa ggt gga ggc cgg atc gtg ctg tat gga gac    2545
Tyr Gln Ile Pro Ser Glu Gly Gly Gly Arg Ile Val Leu Tyr Gly Asp
            835             840             845

tcc aac tgc ttg gat gac agt cac aga cag aag gac tgc ttt tgg ctt    2593
Ser Asn Cys Leu Asp Asp Ser His Arg Gln Lys Asp Cys Phe Trp Leu
            850             855             860

ctg gat gcg ctc ctt cag tac aca tcc tat ggc gtg acc cct ccc agc    2641
Leu Asp Ala Leu Leu Gln Tyr Thr Ser Tyr Gly Val Thr Pro Pro Ser
            865             870             875

ctc agc cat tca ggg aac cgg cag cgc cca cct agc gga gcc ggc ttg    2689
Leu Ser His Ser Gly Asn Arg Gln Arg Pro Pro Ser Gly Ala Gly Leu
    880             885             890

gcc cct cct gaa agg atg gaa gga aac cac ctc cat cgg tac tcc aaa    2737
Ala Pro Pro Glu Arg Met Glu Gly Asn His Leu His Arg Tyr Ser Lys
895             900             905             910

gtt ctt gaa gcc cac ttg gga gac ccg aaa cct cgg ccc ctg cca gcc    2785
Val Leu Glu Ala His Leu Gly Asp Pro Lys Pro Arg Pro Leu Pro Ala
            915             920             925

tgt cca cat ttg tca tgg gcc aag cca cag cct ttg aat gag acg gca    2833
Cys Pro His Leu Ser Trp Ala Lys Pro Gln Pro Leu Asn Glu Thr Ala
            930             935             940

ccc agt aat ctt tgg aaa cat cag aag ctg ctc tcc att gac ctg gac    2881
Pro Ser Asn Leu Trp Lys His Gln Lys Leu Leu Ser Ile Asp Leu Asp
    945             950             955

aaa gta gtg tta ccc aac ttt cga tcc aat cgc cct caa gtg aga cct    2929
Lys Val Val Leu Pro Asn Phe Arg Ser Asn Arg Pro Gln Val Arg Pro
    960             965             970

ttg tcc cct gga gag agt ggt gcc tgg gac att cct gga ggg atc atg    2977
Leu Ser Pro Gly Glu Ser Gly Ala Trp Asp Ile Pro Gly Gly Ile Met
975             980             985             990

cct ggc cgc tac aac cag gag gtg gga cag  acc atc ccc gtc ttc  gcc  3025
Pro Gly Arg Tyr Asn Gln Glu Val Gly Gln Thr Ile Pro Val Phe Ala
            995             1000            1005

ttc ctc gga gcc  atg gtg gcc ctg gcc  ttc ttt gtg gta cag  atc     3070
Phe Leu Gly Ala Met Val Ala Leu Ala Phe Phe Val Val Gln Ile
            1010            1015            1020

agc aag gcc aag  agc cgg ccg aag cgg agg agg ccc agg gca  aag       3115
Ser Lys Ala Lys Ser Arg Pro Lys Arg Arg Arg Pro Arg Ala Lys
            1025            1030            1035

cgt cca caa ctt gca cag cag gcc cac cct gca agg acc cca tca        3160
Arg Pro Gln Leu Ala Gln Gln Ala His Pro Ala Arg Thr Pro Ser
            1040            1045            1050
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gtg tgagcatcgc agtagccagc cacagaagct aacaagcctt gaaccactct          3213
Val

ggtggccaca cagcgcctca gagagcattc tgggaagtgc ctgtttccga ggaccctgtc   3273

tccagcttgt ggctatctta ctgtgttctg cccaggcacc tgatgaggta catcctgcag   3333

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gacagtgcac caaagacaca gagcctggaa gggctgtcgg gacatacttt ctacataacg   3453

ctacaaccct gaccaagcaa agacatgctt gttacaggct attttctata tttattgtgg   3513

gagagtcact ttaaagactg tgctagttgg aaacagagct gttgctgttg tcagtcgagt   3573

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acacactgaa ctgaagggga cttgcgcgga tgtgggagat gcaagccttc gctttatttt   3693

tttataacta tcaactgcca tcatgttttg taatttgggg atcttgattt caccgttgtt   3753

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Ala Pro Cys Pro Ser Cys Ser His Leu Thr Leu Lys Val Glu Phe Ser
            35              40                  45

Ser Thr Val Val Glu Tyr Glu Tyr Ile Val Ala Phe Asn Gly Tyr Phe
        50              55                  60

Thr Ala Lys Ala Arg Asn Ser Phe Ile Ser Ser Ala Leu Lys Ser Ser
65              70              75                  80

Glu Val Glu Asn Trp Arg Ile Ile Pro Arg Asn Asn Pro Ser Ser Asp
                85              90                  95

Tyr Pro Ser Asp Phe Glu Val Ile Gln Ile Lys Glu Lys Gln Lys Ala
            100             105                 110

Gly Leu Leu Thr Leu Glu Asp His Pro Asn Ile Lys Arg Val Thr Pro
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Gln Arg Lys Val Phe Arg Ser Leu Lys Phe Ala Glu Ser Asn Pro Ile
    130   135   140

Val Pro Cys Asn Glu Thr Arg Trp Ser Gln Lys Trp Gln Ser Ser Arg
145   150   155   160

Pro Leu Lys Arg Ala Ser Leu Ser Leu Gly Ser Gly Phe Trp His Ala
            165   170   175

Thr Gly Arg His Ser Ser Arg Arg Leu Leu Arg Ala Ile Pro Arg Gln
            180   185   190

Val Ala Gln Thr Leu Gln Ala Asp Val Leu Trp Gln Met Gly Tyr Thr
        195   200   205

Gly Ala Asn Val Arg Val Ala Val Phe Asp Thr Gly Leu Ser Glu Lys
    210   215   220

His Pro His Phe Lys Asn Val Lys Glu Arg Thr Asn Trp Thr Asn Glu
225   230   235   240

Arg Thr Leu Asp Asp Gly Leu Gly His Gly Thr Phe Val Ala Gly Val
            245   250   255

Ile Ala Ser Met Arg Glu Cys Gln Gly Phe Ala Pro Asp Ala Glu Leu
            260   265   270

His Ile Phe Arg Val Phe Thr Asn Asn Gln Val Ser Tyr Thr Ser Trp
        275   280   285

Phe Leu Asp Ala Phe Asn Tyr Ala Ile Leu Lys Lys Met Asp Val Leu
    290   295   300

Asn Leu Ser Ile Gly Gly Pro Asp Phe Met Asp His Pro Phe Val Asp
305   310   315   320

Lys Val Trp Glu Leu Thr Ala Asn Asn Val Ile Met Val Ser Ala Ile
            325   330   335

Gly Asn Asp Gly Pro Leu Tyr Gly Thr Leu Asn Asn Pro Ala Asp Gln
            340   345   350

Met Asp Val Ile Gly Val Gly Gly Ile Asp Phe Glu Asp Asn Ile Ala
            355   360   365

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Arg Phe Ser Ser Arg Gly Met Thr Thr Trp Glu Leu Pro Gly Gly Tyr
370   375   380

Gly Arg Val Lys Pro Asp Ile Val Thr Tyr Gly Ala Gly Val Arg Gly
385   390   395   400

Ser Gly Val Lys Gly Gly Cys Arg Ala Leu Ser Gly Thr Ser Val Ala
            405   410   415

Ser Pro Val Val Ala Gly Ala Val Thr Leu Leu Val Ser Thr Val Gln
            420   425   430

Lys Arg Glu Leu Val Asn Pro Ala Ser Val Lys Gln Ala Leu Ile Ala
        435   440   445

Ser Ala Arg Arg Leu Pro Gly Val Asn Met Phe Glu Gln Gly His Gly
    450   455   460

Lys Leu Asp Leu Leu Arg Ala Tyr Gln Ile Leu Ser Ser Tyr Lys Pro
465   470   475   480

Gln Ala Ser Leu Ser Pro Ser Tyr Ile Asp Leu Thr Glu Cys Pro Tyr
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Met Trp Pro Tyr Cys Ser Gln Pro Ile Tyr Tyr Gly Gly Met Pro Thr
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Ile Val Asn Val Thr Ile Leu Asn Gly Met Gly Val Thr Gly Arg Ile
        515   520   525

Val Asp Lys Pro Glu Trp Arg Pro Tyr Leu Pro Gln Asn Gly Asp Asn
    530   535   540

Ile Glu Val Ala Phe Ser Tyr Ser Ser Val Leu Trp Pro Trp Ser Gly
545   550   555   560

Tyr Leu Ala Ile Ser Ile Ser Val Thr Lys Lys Ala Ala Ser Trp Glu
            565   570   575

Gly Ile Ala Gln Gly His Ile Met Ile Thr Val Ala Ser Pro Ala Glu
            580   585   590

Thr Glu Leu His Ser Gly Ala Glu His Thr Ser Thr Val Lys Leu Pro
        595   600   605

Ile Lys Val Lys Ile Ile Pro Thr Pro Pro Arg Ser Lys Arg Val Leu
    610   615   620

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Trp Asp Gln Tyr His Asn Leu Arg Tyr Pro Pro Gly Tyr Phe Pro Arg
625   630   635   640

Asp Asn Leu Arg Met Lys Asn Asp Pro Leu Asp Trp Asn Gly Asp His
            645   650   655

Val His Thr Asn Phe Arg Asp Met Tyr Gln His Leu Arg Ser Met Gly
            660   665   670

Tyr Phe Val Glu Val Leu Gly Ala Pro Phe Thr Cys Phe Asp Ala Thr
            675   680   685

Gln Tyr Gly Thr Leu Leu Leu Val Asp Ser Glu Glu Glu Tyr Phe Pro
    690   695   700

Glu Glu Ile Ala Lys Leu Arg Arg Asp Val Asp Asn Gly Leu Ser Leu
705   710   715   720

Val Ile Phe Ser Asp Trp Tyr Asn Thr Ser Val Met Arg Lys Val Lys
            725   730   735

Phe Tyr Asp Glu Asn Thr Arg Gln Trp Trp Met Pro Asp Thr Gly Gly
            740   745   750

Ala Asn Ile Pro Ala Leu Asn Glu Leu Leu Ser Val Trp Asn Met Gly
    755   760   765

Phe Ser Asp Gly Leu Tyr Glu Gly Glu Phe Val Leu Ala Asn His Asp
    770   775   780

Met Tyr Tyr Ala Ser Gly Cys Ser Ile Ala Lys Phe Pro Glu Asp Gly
785   790   795   800

Val Val Ile Thr Gln Thr Phe Lys Asp Gln Gly Leu Glu Val Leu Lys
            805   810   815

Gln Glu Thr Ala Val Val Glu Asn Val Pro Ile Leu Gly Leu Tyr Gln
            820   825   830

Ile Pro Ser Glu Gly Gly Gly Arg Ile Val Leu Tyr Gly Asp Ser Asn
    835   840   845

Cys Leu Asp Asp Ser His Arg Gln Lys Asp Cys Phe Trp Leu Leu Asp
    850   855   860

Ala Leu Leu Gln Tyr Thr Ser Tyr Gly Val Thr Pro Pro Ser Leu Ser
                            Page 18

865   870   875   880

His Ser Gly Asn Arg Gln Arg Pro Pro Ser Gly Ala Gly Leu Ala Pro
              885   890   895

Pro Glu Arg Met Glu Gly Asn His Leu His Arg Tyr Ser Lys Val Leu
          900   905   910

Glu Ala His Leu Gly Asp Pro Lys Pro Arg Pro Leu Pro Ala Cys Pro
          915   920   925

His Leu Ser Trp Ala Lys Pro Gln Pro Leu Asn Glu Thr Ala Pro Ser
    930   935   940

Asn Leu Trp Lys His Gln Lys Leu Leu Ser Ile Asp Leu Asp Lys Val
945   950   955   960

Val Leu Pro Asn Phe Arg Ser Asn Arg Pro Gln Val Arg Pro Leu Ser
              965   970   975

Pro Gly Glu Ser Gly Ala Trp Asp Ile Pro Gly Gly Ile Met Pro Gly
          980   985   990

Arg Tyr Asn Gln Glu Val Gly Gln Thr Ile Pro Val Phe Ala Phe Leu
          995   1000   1005

Gly Ala Met Val Ala Leu Ala Phe Phe Val Val Gln Ile Ser Lys
    1010   1015   1020

Ala Lys Ser Arg Pro Lys Arg Arg Arg Pro Arg Ala Lys Arg Pro
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Gln Leu Ala Gln Gln Ala His Pro Ala Arg Thr Pro Ser Val
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gcggaggcgc cgttatcccg ggcccgccgg ccctgagctc ccggcggcgc agattggctc   180

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acagtggttg attgatcaac cccattggac gttggttctg tggtacaaat ggagtacagg      240

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aaagaaatga aagcctctct tcaggctgaa ccacaaaagg ccatgggatt taacttttat      360

ttatgttggg caagactgta agatggctga tcagtaatgt tgcagctttt agctgaaaca      420

aaaattcact tttaatcaag aagaaaaag tgtgatttga atatatgcaa ttttatgatc       480
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atattcgctt gtgacc atg aag ctt gtc aac atc tgg ctg ctt ctg ctc gtg      532
               Met Lys Leu Val Asn Ile Trp Leu Leu Leu Leu Val
               1               5                   10
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gtt ttg ctc tgt ggg aag aaa cat ctg ggc gac aga ctg gaa aag aaa       580
Val Leu Leu Cys Gly Lys Lys His Leu Gly Asp Arg Leu Glu Lys Lys
         15              20              25
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tct ttt gaa aag gcc cca tgc cct ggc tgt tcc cac ctg act ttg aag       628
Ser Phe Glu Lys Ala Pro Cys Pro Gly Cys Ser His Leu Thr Leu Lys
     30              35              40
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gtg gaa ttc tca tca aca gtt gtg gaa tat gaa tat att gtg gct ttc       676
Val Glu Phe Ser Ser Thr Val Val Glu Tyr Glu Tyr Ile Val Ala Phe
45              50              55              60
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aat gga tac ttt aca gcc aaa gct aga aat tca ttt att tca agt gcc       724
Asn Gly Tyr Phe Thr Ala Lys Ala Arg Asn Ser Phe Ile Ser Ser Ala
                 65              70              75
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ctg aag agc agt gaa gta gac aat tgg aga att ata cct cga aac aat       772
Leu Lys Ser Ser Glu Val Asp Asn Trp Arg Ile Ile Pro Arg Asn Asn
         80              85              90
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cca tcc agt gac tac cct agt gat ttt gag gtg att cag ata aaa gaa       820
Pro Ser Ser Asp Tyr Pro Ser Asp Phe Glu Val Ile Gln Ile Lys Glu
         95              100             105
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aaa cag aaa gcg ggg ctg cta aca ctt gaa gat cat cca aac atc aaa       868
Lys Gln Lys Ala Gly Leu Leu Thr Leu Glu Asp His Pro Asn Ile Lys
110             115             120
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cgg gtc acg ccc caa cga aaa gtc ttt cgt tcc ctc aag tat gct gaa       916
Arg Val Thr Pro Gln Arg Lys Val Phe Arg Ser Leu Lys Tyr Ala Glu
125             130             135             140
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tct gac ccc aca gta ccc tgc aat gaa acc cgg tgg agc cag aag tgg       964
Ser Asp Pro Thr Val Pro Cys Asn Glu Thr Arg Trp Ser Gln Lys Trp
                 145             150             155
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caa tca tca cgt ccc ctg cga aga gcc agc ctc tcc ctg ggc tct ggc      1012
Gln Ser Ser Arg Pro Leu Arg Arg Ala Ser Leu Ser Leu Gly Ser Gly
                 160             165             170
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ttc tgg cat gct acg gga agg cat tcg agc aga cgg ctg ctg aga gcc      1060
Phe Trp His Ala Thr Gly Arg His Ser Ser Arg Arg Leu Leu Arg Ala
         175             180             185
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atc ccg cgc cag gtt gcc cag aca ctg cag gca gat gtg ctc tgg cag      1108
Ile Pro Arg Gln Val Ala Gln Thr Leu Gln Ala Asp Val Leu Trp Gln
         190             195             200
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atg gga tat aca ggt gct aat gta aga gtt gct gtt ttt gac act ggg      1156
Met Gly Tyr Thr Gly Ala Asn Val Arg Val Ala Val Phe Asp Thr Gly
205                     210                 215                 220

ctg agc gag aag cat ccc cac ttc aaa aat gtg aag gag aga acc aac      1204
Leu Ser Glu Lys His Pro His Phe Lys Asn Val Lys Glu Arg Thr Asn
                    225                 230                 235

tgg acc aac gag cga acg ctg gac gat ggg ttg ggc cat ggc aca ttc      1252
Trp Thr Asn Glu Arg Thr Leu Asp Asp Gly Leu Gly His Gly Thr Phe
                240                 245                 250

gtg gca ggt gtg ata gcc agc atg agg gag tgc caa gga ttt gct cca      1300
Val Ala Gly Val Ile Ala Ser Met Arg Glu Cys Gln Gly Phe Ala Pro
            255                 260                 265

gat gca gaa ctt cac att ttc agg gtc ttt acc aat aat cag gta tct      1348
Asp Ala Glu Leu His Ile Phe Arg Val Phe Thr Asn Asn Gln Val Ser
270                 275                 280

tac aca tct tgg ttt ttg gac gcc ttc aac tat gcc att tta aag aag      1396
Tyr Thr Ser Trp Phe Leu Asp Ala Phe Asn Tyr Ala Ile Leu Lys Lys
285                 290                 295                 300

atc gac gtg tta aac ctc agc atc ggc ggc ccg gac ttc atg gat cat      1444
Ile Asp Val Leu Asn Leu Ser Ile Gly Gly Pro Asp Phe Met Asp His
                305                 310                 315

ccg ttt gtt gac aag gtg tgg gaa tta aca gct aac aat gta atc atg      1492
Pro Phe Val Asp Lys Val Trp Glu Leu Thr Ala Asn Asn Val Ile Met
            320                 325                 330

gtt tct gct att ggc aat gac gga cct ctt tat ggc act ctg aat aac      1540
Val Ser Ala Ile Gly Asn Asp Gly Pro Leu Tyr Gly Thr Leu Asn Asn
            335                 340                 345


cct gct gat caa atg gat gtg att gga gta ggc ggc att gac ttt gaa      1588
Pro Ala Asp Gln Met Asp Val Ile Gly Val Gly Gly Ile Asp Phe Glu
        350                 355                 360

gat aac atc gcc cgc ttt tct tca agg gga atg act acc tgg gag cta      1636
Asp Asn Ile Ala Arg Phe Ser Ser Arg Gly Met Thr Thr Trp Glu Leu
365                 370                 375                 380

cca gga ggc tac ggt cgc atg aaa cct gac att gtc acc tat ggt gct      1684
Pro Gly Gly Tyr Gly Arg Met Lys Pro Asp Ile Val Thr Tyr Gly Ala
                385                 390                 395

ggc gtg cgg ggt tct ggc gtg aaa ggg ggg tgc cgg gcc ctc tca ggg      1732
Gly Val Arg Gly Ser Gly Val Lys Gly Gly Cys Arg Ala Leu Ser Gly
            400                 405                 410

acc agt gtt gct tct cca gtg gtt gca ggt gct gtc acc ttg tta gtg      1780
Thr Ser Val Ala Ser Pro Val Val Ala Gly Ala Val Thr Leu Leu Val
            415                 420                 425

agc aca gtc cag aag cgt gag ctg gtg aat ccc gcc agt atg aag cag      1828
Ser Thr Val Gln Lys Arg Glu Leu Val Asn Pro Ala Ser Met Lys Gln
430                 435                 440

gcc ctg atc gcg tca gcc cgg agg ctc ccc ggg gtc aac atg ttt gag      1876
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Ala Leu Ile Ala Ser Ala Arg Arg Leu Pro Gly Val Asn Met Phe Glu
445            450            455            460
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caa ggc cac ggc aag ctc gat ctg ctc aga gcc tat cag atc ctc aac    1924
Gln Gly His Gly Lys Leu Asp Leu Leu Arg Ala Tyr Gln Ile Leu Asn
                465            470            475
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agc tac aag cca cag gca agt ttg agc ccc agc tac ata gat ctg act    1972
Ser Tyr Lys Pro Gln Ala Ser Leu Ser Pro Ser Tyr Ile Asp Leu Thr
                480            485            490
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gag tgt ccc tac atg tgg ccc tac tgc tcc cag ccc atc tac tat gga    2020
Glu Cys Pro Tyr Met Trp Pro Tyr Cys Ser Gln Pro Ile Tyr Tyr Gly
            495            500            505
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gga atg ccg aca gtt gtt aat gtc acc atc ctc aac ggc atg gga gtc    2068
Gly Met Pro Thr Val Val Asn Val Thr Ile Leu Asn Gly Met Gly Val
        510            515            520
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aca gga aga att gta gat aag cct gac tgg cag ccc tat ttg cca cag    2116
Thr Gly Arg Ile Val Asp Lys Pro Asp Trp Gln Pro Tyr Leu Pro Gln
525            530            535            540
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aac gga gac aac att gaa gtt gcc ttc tcc tac tcc tcg gtc tta tgg    2164
Asn Gly Asp Asn Ile Glu Val Ala Phe Ser Tyr Ser Ser Val Leu Trp
                545            550            555
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cct tgg tcg ggc tac ctg gcc atc tcc att tct gtg acc aag aaa gcg    2212
Pro Trp Ser Gly Tyr Leu Ala Ile Ser Ile Ser Val Thr Lys Lys Ala
            560            565            570
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gct tcc tgg gaa ggc att gct cag ggc cat gtc atg atc act gtg gct    2260
Ala Ser Trp Glu Gly Ile Ala Gln Gly His Val Met Ile Thr Val Ala
            575            580            585
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tcc cca gca gag aca gag tca aaa aat ggt gca gaa cag act tca aca    2308
Ser Pro Ala Glu Thr Glu Ser Lys Asn Gly Ala Glu Gln Thr Ser Thr
        590            595            600
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gta aag ctc ccc att aag gtg aag ata att cct act ccc ccg cga agc    2356
Val Lys Leu Pro Ile Lys Val Lys Ile Ile Pro Thr Pro Pro Arg Ser
605            610            615            620
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aag aga gtt ctc tgg gat cag tac cac aac ctc cgc tat cca cct ggc    2404
Lys Arg Val Leu Trp Asp Gln Tyr His Asn Leu Arg Tyr Pro Pro Gly
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tat ttc ccc agg gat aat tta agg atg aag aat gac cct tta gac tgg    2452
Tyr Phe Pro Arg Asp Asn Leu Arg Met Lys Asn Asp Pro Leu Asp Trp
            640            645            650
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aat ggt gat cac atc cac acc aat ttc agg gat atg tac cag cat ctg    2500
Asn Gly Asp His Ile His Thr Asn Phe Arg Asp Met Tyr Gln His Leu
            655            660            665
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aga agc atg ggc tac ttt gta gag gtc ctc ggg gcc ccc ttc acg tgt    2548
Arg Ser Met Gly Tyr Phe Val Glu Val Leu Gly Ala Pro Phe Thr Cys
        670            675            680
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ttt gat gcc agt cag tat ggc act ttg ctg atg gtg gac agt gag gag    2596
Phe Asp Ala Ser Gln Tyr Gly Thr Leu Leu Met Val Asp Ser Glu Glu
685            690            695            700
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gag tac ttc cct gaa gag atc gcc aag ctc cgg agg gac gtg gac aac    2644
Glu Tyr Phe Pro Glu Glu Ile Ala Lys Leu Arg Arg Asp Val Asp Asn
            705                 710                 715

ggc ctc tcg ctc gtc atc ttc agt gac tgg tac aac act tct gtt atg    2692
Gly Leu Ser Leu Val Ile Phe Ser Asp Trp Tyr Asn Thr Ser Val Met
            720                 725                 730

aga aaa gtg aag ttt tat gat gaa aac aca agg cag tgg tgg atg ccg    2740
Arg Lys Val Lys Phe Tyr Asp Glu Asn Thr Arg Gln Trp Trp Met Pro
            735                 740                 745

gat acc gga gga gct aac atc cca gct ctg aat gag ctg ctg tct gtg    2788
Asp Thr Gly Gly Ala Asn Ile Pro Ala Leu Asn Glu Leu Leu Ser Val
            750                 755                 760

tgg aac atg ggg ttc agc gat ggc ctg tat gaa ggg gag ttc acc ctg    2836
Trp Asn Met Gly Phe Ser Asp Gly Leu Tyr Glu Gly Glu Phe Thr Leu
765                 770                 775                 780

gcc aac cat gac atg tat tat gcg tca ggg tgc agc atc gcg aag ttt    2884
Ala Asn His Asp Met Tyr Tyr Ala Ser Gly Cys Ser Ile Ala Lys Phe
                785                 790                 795

cca gaa gat ggc gtc gtg ata aca cag act ttc aag gac caa gga ttg    2932
Pro Glu Asp Gly Val Val Ile Thr Gln Thr Phe Lys Asp Gln Gly Leu
            800                 805                 810


gag gtt tta aag cag gaa aca gca gtt gtt gaa aac gtc ccc att ttg    2980
Glu Val Leu Lys Gln Glu Thr Ala Val Val Glu Asn Val Pro Ile Leu
            815                 820                 825

gga ctt tat cag att cca gct gag ggt gga ggc cgg att gta ctg tat    3028
Gly Leu Tyr Gln Ile Pro Ala Glu Gly Gly Gly Arg Ile Val Leu Tyr
            830                 835                 840

ggg gac tcc aat tgc ttg gat gac agt cac cga cag aag gac tgc ttt    3076
Gly Asp Ser Asn Cys Leu Asp Asp Ser His Arg Gln Lys Asp Cys Phe
845                 850                 855                 860

tgg ctt ctg gat gcc ctc ctc cag tac aca tcg tat ggg gtg aca ccg    3124
Trp Leu Leu Asp Ala Leu Leu Gln Tyr Thr Ser Tyr Gly Val Thr Pro
                865                 870                 875

cct agc ctc agt cac tct ggg aac cgc cag cgc cct ccc agt gga gca    3172
Pro Ser Leu Ser His Ser Gly Asn Arg Gln Arg Pro Pro Ser Gly Ala
                880                 885                 890

ggc tca gtc act cca gag agg atg gaa gga aac cat ctt cat cgg tac    3220
Gly Ser Val Thr Pro Glu Arg Met Glu Gly Asn His Leu His Arg Tyr
            895                 900                 905

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Ser Lys Val Leu Glu Ala His Leu Gly Asp Pro Lys Pro Arg Pro Leu
910                 915                 920

cca gcc tgt cca cgc ttg tct tgg gcc aag cca cag cct tta aac gag    3316
Pro Ala Cys Pro Arg Leu Ser Trp Ala Lys Pro Gln Pro Leu Asn Glu
925                 930                 935                 940

acg gcg ccc agt aac ctt tgg aaa cat cag aag cta ctc tcc att gac    3364
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                          945                 950                 955

ctg gac aag gtg gtg tta ccc aac ttt cga tcg aat cgc cct caa gtg          3412
Leu Asp Lys Val Val Leu Pro Asn Phe Arg Ser Asn Arg Pro Gln Val
            960                 965                 970

agg ccc ttg tcc cct gga gag agc ggc gcc tgg gac att cct gga ggg          3460
Arg Pro Leu Ser Pro Gly Glu Ser Gly Ala Trp Asp Ile Pro Gly Gly
            975                 980                 985

atc atg cct ggc cgc tac aac cag gag gtg ggc cag  acc att cct gtc         3508
Ile Met Pro Gly Arg Tyr Asn Gln Glu Val Gly Gln  Thr Ile Pro Val
            990                 995                 1000

ttt  gcc ttc ctg gga gcc  atg gtg gtc ctg gcc  ttc ttt gtg gta          3553
Phe  Ala Phe Leu Gly Ala  Met Val Val Leu Ala  Phe Phe Val Val
1005                 1010                 1015

caa atc aac aag gcc aag agc agg ccg aag cgg agg aag ccc agg              3598
Gln Ile Asn Lys Ala Lys Ser Arg Pro Lys Arg Arg Lys Pro Arg
1020                 1025                 1030

gtg aag cgc ccg cag ctc atg cag cag gtt cac ccg cca aag acc              3643
Val Lys Arg Pro Gln Leu Met Gln Gln Val His Pro Pro Lys Thr
1035                 1040                 1045

cct tcg gtg tgaccggcag cctggctgac cgtgagggcc agagagagcc               3692
Pro Ser Val
1050


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cagaggctcc tggtacatcg agaagattcc tgtggatccc gtcaggaggg acttagtggc          3872

tctgccgcca gtgagacttc ccgccggcag ctgtgcgcac caaagactcg ggagaactgg          3932

aaaggctgtc tggggtcttc tgactgcagg ggaaggatgt actttccaaa caaatgatac          3992

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tttttgtaag tatcacctgc caccatgttt tgtaatttga ggtcttgatt tcaccattgt          4292

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Ala Pro Cys Pro Gly Cys Ser His Leu Thr Leu Lys Val Glu Phe Ser
        35   40   45

Ser Thr Val Val Glu Tyr Glu Tyr Ile Val Ala Phe Asn Gly Tyr Phe
    50   55   60

Thr Ala Lys Ala Arg Asn Ser Phe Ile Ser Ser Ala Leu Lys Ser Ser
65   70   75   80

Glu Val Asp Asn Trp Arg Ile Ile Pro Arg Asn Asn Pro Ser Ser Asp
            85   90   95

Tyr Pro Ser Asp Phe Glu Val Ile Gln Ile Lys Glu Lys Gln Lys Ala
            100   105   110

Gly Leu Leu Thr Leu Glu Asp His Pro Asn Ile Lys Arg Val Thr Pro
        115   120   125

Gln Arg Lys Val Phe Arg Ser Leu Lys Tyr Ala Glu Ser Asp Pro Thr
    130   135   140

Val Pro Cys Asn Glu Thr Arg Trp Ser Gln Lys Trp Gln Ser Ser Arg
145   150   155   160

Pro Leu Arg Arg Ala Ser Leu Ser Leu Gly Ser Gly Phe Trp His Ala
            165   170   175

Thr Gly Arg His Ser Ser Arg Arg Leu Leu Arg Ala Ile Pro Arg Gln
            180   185   190

Val Ala Gln Thr Leu Gln Ala Asp Val Leu Trp Gln Met Gly Tyr Thr
    195   200   205

Gly Ala Asn Val Arg Val Ala Val Phe Asp Thr Gly Leu Ser Glu Lys
210   215   220

His Pro His Phe Lys Asn Val Lys Glu Arg Thr Asn Trp Thr Asn Glu
225   230   235   240

Arg Thr Leu Asp Asp Gly Leu Gly His Gly Thr Phe Val Ala Gly Val
            245   250   255

Ile Ala Ser Met Arg Glu Cys Gln Gly Phe Ala Pro Asp Ala Glu Leu
                            Page 25

                260   265   270

His Ile Phe Arg Val Phe Thr Asn Asn Gln Val Ser Tyr Thr Ser Trp
        275   280   285

Phe Leu Asp Ala Phe Asn Tyr Ala Ile Leu Lys Lys Ile Asp Val Leu
    290   295   300

Asn Leu Ser Ile Gly Gly Pro Asp Phe Met Asp His Pro Phe Val Asp
305   310   315   320

Lys Val Trp Glu Leu Thr Ala Asn Asn Val Ile Met Val Ser Ala Ile
            325   330   335

Gly Asn Asp Gly Pro Leu Tyr Gly Thr Leu Asn Asn Pro Ala Asp Gln
            340   345   350

Met Asp Val Ile Gly Val Gly Gly Ile Asp Phe Glu Asp Asn Ile Ala
        355   360   365

Arg Phe Ser Ser Arg Gly Met Thr Thr Trp Glu Leu Pro Gly Gly Tyr
    370   375   380

Gly Arg Met Lys Pro Asp Ile Val Thr Tyr Gly Ala Gly Val Arg Gly
385   390   395   400

Ser Gly Val Lys Gly Gly Cys Arg Ala Leu Ser Gly Thr Ser Val Ala
            405   410   415

Ser Pro Val Val Ala Gly Ala Val Thr Leu Leu Val Ser Thr Val Gln
            420   425   430

Lys Arg Glu Leu Val Asn Pro Ala Ser Met Lys Gln Ala Leu Ile Ala
            435   440   445

Ser Ala Arg Arg Leu Pro Gly Val Asn Met Phe Glu Gln Gly His Gly
    450   455   460

Lys Leu Asp Leu Leu Arg Ala Tyr Gln Ile Leu Asn Ser Tyr Lys Pro
465   470   475   480

Gln Ala Ser Leu Ser Pro Ser Tyr Ile Asp Leu Thr Glu Cys Pro Tyr
            485   490   495

Met Trp Pro Tyr Cys Ser Gln Pro Ile Tyr Tyr Gly Gly Met Pro Thr
            500   505   510

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Val Val Asn Val Thr Ile Leu Asn Gly Met Gly Val Thr Gly Arg Ile
     515   520   525

Val Asp Lys Pro Asp Trp Gln Pro Tyr Leu Pro Gln Asn Gly Asp Asn
   530   535   540

Ile Glu Val Ala Phe Ser Tyr Ser Ser Val Leu Trp Pro Trp Ser Gly
545   550   555   560

Tyr Leu Ala Ile Ser Ile Ser Val Thr Lys Lys Ala Ala Ser Trp Glu
     565   570   575

Gly Ile Ala Gln Gly His Val Met Ile Thr Val Ala Ser Pro Ala Glu
     580   585   590

Thr Glu Ser Lys Asn Gly Ala Glu Gln Thr Ser Thr Val Lys Leu Pro
     595   600   605

Ile Lys Val Lys Ile Ile Pro Thr Pro Pro Arg Ser Lys Arg Val Leu
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Trp Asp Gln Tyr His Asn Leu Arg Tyr Pro Pro Gly Tyr Phe Pro Arg
625   630   635   640

Asp Asn Leu Arg Met Lys Asn Asp Pro Leu Asp Trp Asn Gly Asp His
     645   650   655

Ile His Thr Asn Phe Arg Asp Met Tyr Gln His Leu Arg Ser Met Gly
     660   665   670

Tyr Phe Val Glu Val Leu Gly Ala Pro Phe Thr Cys Phe Asp Ala Ser
     675   680   685

Gln Tyr Gly Thr Leu Leu Met Val Asp Ser Glu Glu Glu Tyr Phe Pro
     690   695   700

Glu Glu Ile Ala Lys Leu Arg Arg Asp Val Asp Asn Gly Leu Ser Leu
705   710   715   720

Val Ile Phe Ser Asp Trp Tyr Asn Thr Ser Val Met Arg Lys Val Lys
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Phe Tyr Asp Glu Asn Thr Arg Gln Trp Trp Met Pro Asp Thr Gly Gly
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Ala Asn Ile Pro Ala Leu Asn Glu Leu Leu Ser Val Trp Asn Met Gly
     755   760   765

Phe Ser Asp Gly Leu Tyr Glu Gly Glu Phe Thr Leu Ala Asn His Asp
    770   775   780

Met Tyr Tyr Ala Ser Gly Cys Ser Ile Ala Lys Phe Pro Glu Asp Gly
785   790   795   800

Val Val Ile Thr Gln Thr Phe Lys Asp Gln Gly Leu Glu Val Leu Lys
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Gln Glu Thr Ala Val Val Glu Asn Val Pro Ile Leu Gly Leu Tyr Gln
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Ile Pro Ala Glu Gly Gly Gly Arg Ile Val Leu Tyr Gly Asp Ser Asn
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Cys Leu Asp Asp Ser His Arg Gln Lys Asp Cys Phe Trp Leu Leu Asp
    850   855   860

Ala Leu Leu Gln Tyr Thr Ser Tyr Gly Val Thr Pro Pro Ser Leu Ser
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His Ser Gly Asn Arg Gln Arg Pro Pro Ser Gly Ala Gly Ser Val Thr
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Pro Glu Arg Met Glu Gly Asn His Leu His Arg Tyr Ser Lys Val Leu
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Glu Ala His Leu Gly Asp Pro Lys Pro Arg Pro Leu Pro Ala Cys Pro
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Arg Leu Ser Trp Ala Lys Pro Gln Pro Leu Asn Glu Thr Ala Pro Ser
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Asn Leu Trp Lys His Gln Lys Leu Leu Ser Ile Asp Leu Asp Lys Val
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Val Leu Pro Asn Phe Arg Ser Asn Arg Pro Gln Val Arg Pro Leu Ser
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Pro Gly Glu Ser Gly Ala Trp Asp Ile Pro Gly Gly Ile Met Pro Gly
            980   985   990

Arg Tyr Asn Gln Glu Val Gly Gln Thr Ile Pro Val Phe Ala Phe Leu
        995   1000   1005

Gly Ala Met Val Val Leu Ala Phe Phe Val Val Gln Ile Asn Lys

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Gln Leu Met Gln Gln Val His Pro Pro Lys Thr Pro Ser Val
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<213>  Artificial Sequence

<220>
<223>  Primer

<400>  22
gggatatgct tagcattgac                                       20


<210>  23
<211>  20
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  Primer

<400>  23
agccctatta cctgaacctg                                       20


<210>  24
<211>  20
<212>  DNA
<213>  Artificial Sequence
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<220>
<223>   Primer

<400>   24
gaatctgaaa gaactccccc   20

<210>   25
<211>   20
<212>   DNA
<213>   Artificial Sequence

<220>
<223>   Primer

<400>   25
ttccgagatt ccatcctacg   20

<210>   26
<211>   20
<212>   DNA
<213>   Artificial Sequence

<220>
<223>   Primer

<400>   26
tgcagctcag caggtctatg   20

<210>   27
<211>   20
<212>   DNA
<213>   Artificial Sequence

<220>
<223>   Primer

<400>   27
tctcctccaa cctcaaccac   20

<210>   28
<211>   22
<212>   DNA
<213>   Artificial Sequence

<220>
<223>   Primer

<400>   28
ccagcctgtc atcctcaata tc   22

<210>   29
<211>   21
<212>   DNA
<213>   Artificial Sequence

<220>

<223> Primer

<400> 29
ggagccatgg attgcacttt c   21

<210> 30
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 30
aggagctcaa tgtggcagga   20

<210> 31
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 31
gtgaccatga agcttgtcaa catctgg   27

<210> 32
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 32
acactggtcc ctgagagggc ccggca   26

<210> 33
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 33
attgacctgg acaaggtggt g   21

<210> 34
<211> 57
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 34

ggatcctcta gatcagtggt ggtggtggtg gtggtgctcc tggttgtagc ggccagg   57

<210> 35
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 35
ctcgagggag aggctggctc ttcg   24

<210> 36
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 36
ctcgagtgtc tgggcaacct ggcgcggg   28

<210> 37
<211> 14
<212> PRT
<213> Homo sapiens

<400> 37

Lys Ala Gly Ser Arg Gly Leu Thr Ser Leu Ala Asp Thr Phe
1   5   10

<210> 38
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide Substrate

<400> 38

Gly Gly Ala His Asp Ser Asp Gln His Pro His Ser Gly Ser Gly Arg
1   5   10   15

Ser Val Leu Ser Phe Glu Ser Gly Ser Gly Gly
            20   25

<210> 39
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide Substrate

<400> 39

Trp His Ala Thr Gly Arg His Ser Ser Arg Arg Leu Leu Arg Ala Ile
1   5   10   15

Pro Arg

<210> 40
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide Substrate

<400> 40

Trp His Ala Thr Gly Arg His Ser Ser Arg Arg Leu Leu Arg Ala Leu
1   5   10   15

Glu

<210> 41
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide Substrate

<400> 41

Ser Arg Arg Leu Leu Arg Ala Leu Glu
1   5

<210> 42
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide Substrate

<400> 42

Trp Gln Ser Ser Arg Pro Leu Arg Arg Ala Ser Leu Ser Leu Gly Ser
1   5   10   15

Gly

<210> 43
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide Substrate

<400> 43

Arg Ala Ile Pro Arg Gln Val Ala Gln Thr Leu Gln Ala Asp Val
1   5   10   15

<210> 44
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide Substrate

<400> 44

Pro Gln Arg Lys Val Phe Arg Ser Leu
1   5

<210> 45
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide Substrate

<400> 45

Pro Gln Arg Lys Val Phe Arg Ser Leu Lys Tyr Ala Glu Ser Asp
1   5   10   15

<210> 46
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide

<220>
<221> MOD_RES
<222> (1)..(1)
<223> Xaa represents orthoaminobenzoic acid

<220>
<221> MOD_RES
<222> (13)..(13)
<223> Xaa represents 3-nitrotyrosine

<400> 46

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Xaa Val Phe Arg Ser Leu Lys Tyr Ala Glu Ser Asp Xaa Ala
1               5                   10
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<210>   47
<211>   12
<212>   PRT
<213>   Artificial Sequence

<220>
<223>   Peptide


<220>
<221>   MOD_RES
<222>   (1)..(1)
<223>   Xaa represents orthoaminobenzoic acid

<220>
<221>   MOD_RES
<222>   (11)..(11)
<223>   Xaa represents 3-nitrotyrosine

<400>   47
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Xaa Arg Ser Leu Lys Tyr Ala Glu Ser Asp Xaa Ala
1               5                   10
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<210>   48
<211>   16
<212>   PRT
<213>   Homo sapiens

<400>   48
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Lys Ala Gly Ser Arg Gly Leu Thr Ser Leu Ala Asp Thr Phe Glu His
1               5                   10                  15
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<210>   49
<211>   16
<212>   PRT
<213>   Rattus sp.

<400>   49
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Lys Ala Gly Ser Arg Gly Leu Thr Thr Thr Ser Leu Ala Asp Thr Phe
1               5                   10                  15
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```
<210>   50
<211>   16
<212>   PRT
<213>   Homo sapiens

<400>   50
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Arg His Ser Ser Arg Arg Leu Leu Arg Ala Ile Pro Arg Gln Val Ala
1               5                   10                  15
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<210> 51
<211> 16
<212> PRT
<213> Homo sapiens

<400> 51

Arg Lys Val Phe Arg Ser Leu Lys Tyr Ala Glu Ser Asp Pro Thr Val
1   5   10   15

<210> 52
<211> 16
<212> PRT
<213> Homo sapiens

<400> 52

Thr Pro Gln Arg Lys Val Phe Arg Ser Leu Lys Tyr Ala Glu Ser Asp
1   5   10   15

<210> 53
<211> 16
<212> PRT
<213> Homo sapiens

<400> 53

Val Thr Pro Gln Arg Lys Val Phe Arg Ser Leu Lys Lys Tyr Ala Glu
1   5   10   15

<210> 54
<211> 16
<212> PRT
<213> Homo sapiens

<400> 54

Ser Gly Ser Gly Arg Ser Val Leu Ser Phe Glu Ser Gly Ser Gly Gly
1   5   10   15

<210> 55
<211> 16
<212> PRT
<213> Homo sapiens

<400> 55

His Ser Pro Gly Arg Asn Val Leu Gly Thr Glu Ser Arg Asp Gly Pro
1   5   10   15

<210> 56
<211> 16
<212> PRT
<213> Rattus sp.

<400> 56

Ala Ser Val Gly Arg Leu Ala Leu Ser Gln Glu Glu Pro Ala Pro Leu

<210> 57
<211> 16
<212> PRT
<213> Homo sapiens

<400> 57

Arg Ile Ser Asp Arg Asp Tyr Met Gly Trp Met Asp Phe Gly Arg Arg
1   5   10   15

<210> 58
<211> 16
<212> PRT
<213> Rattus sp.

<400> 58

Asp Pro Arg Leu Arg Gln Phe Leu Gln Lys Ser Leu Ala Ala Ala Thr
1   5   10   15

<210> 59
<211> 16
<212> PRT
<213> Bovis sp.

<400> 59

Leu Leu Lys Glu Leu Gln Asp Leu Ala Leu Gln Gly Ala Lys Glu Arg
1   5   10   15

<210> 60
<211> 16
<212> PRT
<213> Bovis sp.

<400> 60

Met Ala Arg Ala Pro Gln Val Leu Phe Arg Gly Gly Lys Ser Gly Glu
1   5   10   15

<210> 64
<211> 16
<212> PRT
<213> Bovis sp.

<400> 61

Glu Leu Glu Asn Leu Ala Ala Met Asp Leu Glu Leu Gln Lys Ile Ala
1   5   10   15

<210> 62
<211> 16
<212> PRT
<213> Bovis sp.

<400> 62

Ala Ala Met Asp Leu Glu Leu Gln Lys Ile Ala Glu Lys Phe Ser Gly
1   5   10   15

<210> 63
<211> 16
<212> PRT
<213> Rattus sp.

<400> 63

Lys Ser Ser Phe Thr Asn Val Thr Ser Pro Val Val Leu Thr Asn Tyr
1   5   10   15

<210> 64
<211> 16
<212> PRT
<213> Rattus sp.

<400> 64

Lys Ser Gln Thr Pro Leu Val Thr Leu Phe Lys Asn Ala Ile Ile Lys
1   5   10   15

<210> 65
<211> 16
<212> PRT
<213> Rattus sp.

<400> 65

Ser Gln Thr Pro Leu Val Thr Leu Phe Lys Asn Ala Ile Ile Lys Asn
1   5   10   15

<210> 66
<211> 16
<212> PRT
<213> Rattus sp.

<400> 66

Gly Pro Ala Arg Glu Leu Leu Leu Arg Leu Val Gln Leu Ala Gly Thr
1   5   10   15

<210> 67
<211> 16
<212> PRT
<213> Homo sapiens

<400> 67

Leu Leu Arg Lys Lys Arg Thr Thr Ser Ala Glu Lys Asn Thr Cys Gln
1   5   10   15

<210> 68

<211> 16
<212> PRT
<213> Homo sapiens

<400> 68

Glu Glu Ile Ser Glu Val Lys Met Asp Ala Glu Phe Arg His Asp Ser
1   5   10   15

<210> 69
<211> 16
<212> PRT
<213> Homo sapiens

<400> 69

Glu Glu Ile Ser Glu Val Asn Leu Asp Ala Glu Phe Arg His Asp Ser
1   5   10   15

<210> 70
<211> 16
<212> PRT
<213> Homo sapiens

<400> 70

Ile Ser Glu Val Lys Met Asp Ala Glu Phe Arg His Asp Ser Gly Tyr
1   5   10   15

<210> 71
<211> 16
<212> PRT
<213> Homo sapiens

<400> 71

Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val
1   5   10   15

<210> 72
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide substrate

<400> 72

Ser Ser Arg Arg Leu Leu Arg Ala Ile Glu
1   5   10

<210> 73
<211> 12
<212> PRT
<213> Artificial sequence

<220>

<223> Peptide Substrate

<400> 73

Ser Gly Ser Gly Arg Ser Val Leu Ser Phe Glu Ser
1   5   10

<210> 74
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide Substrate

<220>
<221> MOD_RES
<222> (1)..(1)
<223> Xaa represents orthoaminobenzoic acid

<220>
<221> MOD_RES
<222> (13)..(13)
<223> Xaa represents 3-nitrotyrosine

<400> 74

Xaa Arg His Ser Ser Arg Arg Leu Leu Arg Ala Ile Xaa Ala
1   5   10

<210> 75
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide Substrate

<220>
<221> MOD_RES
<222> (1)..(1)
<223> Xaa represents orthoaminobenzoic acid

<220>
<221> MOD_RES
<222> (11)..(11)
<223> Xaa represents 3-nitrotyrosine

<400> 75

Xaa Ser Arg Arg Leu Leu Arg Ala Leu Glu Xaa Ala
1   5   10

<210> 76
<211> 15
<212> PRT
<213> Artificial Sequence

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<220>
<223>  Peptide Substrate


<220>
<221>  MOD_RES
<222>  (1)..(1)
<223>  Xaa represents orthoaminobenzoic acid

<220>
<221>  MOD_RES
<222>  (14)..(14)
<223>  Xaa represents 3-nitrotyrosine

<400>  76

Xaa Asn Gly Pro Lys Ala Gly Ser Arg Gly Leu Thr Ser Xaa Ala
1               5                   10                  15


<210>  77
<211>  13
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Consensus sequence for growth factors

<400>  77

Cys Leu Asp Asp Ser His Arg Gln Lys Asp Cys Phe Trp
1               5                   10


<210>  78
<211>  9
<212>  PRT
<213>  Homo sapiens

<400>  78

Gly Cys Met Leu Ala Ala Pro Met Lys
1               5


<210>  79
<211>  18
<212>  PRT
<213>  Homo sapiens

<400>  79

Arg Gly Leu Thr Ser Leu Ala Asp Thr Phe Glu His Val Ile Glu Glu
1               5                   10                  15


Leu Leu


<210>  80
<211>  10
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<212>   PRT
<213>   Homo sapiens

<400>   80

Lys Ala Gly Ser Arg Gly Leu Thr Ser Leu
1   5   10

<210>   81
<211>   10
<212>   PRT
<213>   Homo sapiens

<400>   81

Gln Cys Leu Cys Val Lys Thr Thr Ser Gln
1   5   10

<210>   82
<211>   10
<212>   PRT
<213>   Homo sapiens

<400>   82

Lys Gly Pro Trp Cys Phe Thr Thr Asp Pro
1   5   10

<210>   83
<211>   10
<212>   PRT
<213>   Homo sapiens

<400>   83

Lys Ser Gln Thr Pro Leu Val Thr Leu Phe
1   5   10

<210>   84
<211>   10
<212>   PRT
<213>   Homo sapiens

<400>   84

Leu Leu Arg Lys Lys Arg Thr Thr Ser Ala
1   5   10

<210>   85
<211>   10
<212>   PRT
<213>   Homo sapiens

<400>   85

Val Gly Gly Val Val Ile Ala Thr Val Ile
1   5   10

<210> 86
<211> 8
<212> PRT
<213> Mus sp.

<400> 86

Arg Gly Leu Thr Thr Thr Ser Leu
1   5

<210> 87
<211> 11
<212> PRT
<213> Sus sp.

<400> 78

Arg Gly Leu Thr Ser Ser Ser Ser Ser Ser Leu
1   5   10

<210> 88
<211> 10
<212> PRT
<213> Homo sapiens

<400> 88

Arg Asn Asn Pro Ser Ser Asp Tyr Pro Ser
1   5   10

<210> 89
<211> 8
<212> PRT
<213> Homo sapiens

<400> 89

Arg His Ser Ser Arg Arg Leu Leu
1   5

<210> 90
<211> 4
<212> PRT
<213> Homo sapiens

<400> 90

Arg Arg Leu Leu
1

<210> 91
<211> 13
<212> PRT
<213> Artificial sequence

<220>
<223> Fragment resulting from cloning

<400> 91

Pro Gly Arg Tyr Asn Gln Glu His His His His His His
1   5   10

<210> 92
<211> 12
<212> PRT
<213> Homo sapiens

<400> 92

Leu Val Val Leu Leu Cys Gly Lys Lys His Leu Gly
1   5   10

<210> 93
<211> 19
<212> PRT
<213> Homo sapiens

<400> 93

Lys Tyr Ala Glu Ser Asp Pro Thr Val Pro Cys Asn Glu Thr Arg Trp
1   5   10   15

Ser Gln Lys

<210> 94
<211> 8
<212> PRT
<213> Homo sapiens

<400> 94

Arg Lys Val Phe Arg Ser Leu Lys
1   5

<210> 95
<211> 7
<212> PRT
<213> Homo sapiens

<400> 95

Gly Lys Lys Arg Lys Val Phe
1   5

<210> 96
<211> 8
<212> PRT
<213> Homo sapiens

<400> 96

Gly Lys Lys Arg Lys Val Phe Arg
1   5

<210> 97
<211> 10
<212> PRT
<213> Homo sapiens

<400> 97

Gly Lys Lys Arg Lys Val Phe Arg Ser Leu
1   5   10

<210> 98
<211> 11
<212> PRT
<213> Homo sapiens

<400> 98

Gly Lys Lys Arg Lys Val Phe Arg Ser Leu Lys
1   5   10

<210> 99
<211> 6
<212> PRT
<213> Homo sapiens

<400> 99

Arg Gly Leu Thr Ser Leu
1   5

<210> 100
<211> 4
<212> PRT
<213> Homo sapiens

<400> 100

Arg Ser Leu Lys
1

<210> 101
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Fluorescent candidate substrate

<220>
<221> VARIANT
<222> (1)..(1)
<223> Xaa represents Abz

<400> 101

Xaa Val Phe Arg Ser Leu Lys
1   5

<210> 102
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> Fluorescent candidate substrate

<220>
<221> VARIANT
<222> (1)..(1)
<223> Xaa represents Abz

<400> 102

Xaa Arg Ser Leu Lys
1   5

<210> 103
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> Non fluorescent candidate substrate

<220>
<221> VARIANT
<222> (6)..(6)
<223> Xaa represents Y(NO2)

<400> 103

Tyr Ala Glu Ser Asp Xaa Ala
1   5

<210> 104
<211> 8
<212> PRT
<213> Homo sapiens

<400> 104

Arg Arg Leu Leu Arg Ala Ile Pro
1   5

<210> 105
<211> 8
<212> PRT
<213> Homo sapiens

<400> 105

Arg Ser Leu Lys Tyr Ala Glu Ser
1   5

<210>   106
<211>   6
<212>   PRT
<213>   Homo sapiens

<400>   106

Arg Arg Leu Leu Arg Ala
1   5

<210>   107
<211>   11
<212>   PRT
<213>   Artificial Sequence

<220>
<223>   Fluorogenic substrate

<220>
<221>   VARIANT
<222>   (1)..(1)
<223>   Xaa represents Abz

<220>
<221>   VARIANT
<222>   (11)..(11)
<223>   Xaa represents Y(NO2)

<400>   107

Xaa Arg Ser Leu Lys Tyr Ala Glu Ser Asp Xaa
1   5   10

<210>   108
<211>   12
<212>   PRT
<213>   Homo sapiens

<400>   108

Gln Arg Lys Val Phe Arg Ser Leu Lys Tyr Ala Glu
1   5   10

58

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